

AMENDMENTS TO THE CLAIMS

1. (Original): A method for identifying a subject at risk of melanoma, which comprises detecting the presence or absence of one or more polymorphic variations associated with melanoma in a nucleic acid sample from a subject, wherein the polymorphic variation is detected in a nucleotide sequence selected from the group consisting of

- (a) the nucleotide sequence of SEQ ID NO:1;
- (b) a nucleotide sequence which encodes a polypeptide consisting of the amino acid sequence set forth in Figures 2A to 2G and Figure 3B;
- (c) a nucleotide sequence which encodes a polypeptide that is 90% or more identical to the amino acid sequence set forth in Figures 2A to 2G and Figure 3B;
- (d) a fragment of a nucleotide sequence of (a), (b), or (c); and

the polymorphic variation does not alter the valine at position 599 in the amino acid sequence set forth in Figure 3B;

whereby the presence of the polymorphic variation is indicative of the subject being at risk of melanoma.

2. (Original): The method of claim 1, which further comprises obtaining the nucleic acid sample from the subject.

3. (Original): The method of claim 1, wherein the polymorphic variations is detected at position the one or more polymorphic variations are detected at one or more positions in SEQ ID NO: 1 selected from the group consisting of 146311, 138875, 132526, 128002, 118712, 98846, 98682, 87826, 80400, 76779, 68398 and 64547.

4. (Original): The method of claim 3, wherein a polymorphic variation is detected at position 146311 in SEQ ID NO:1.

5. (Original): The method of claim 3, wherein a polymorphic variation is detected at position 132526 in SEQ ID NO:1.

6. (Original): The method of claim 3, wherein a polymorphic variation is detected at position 128002 in SEQ ID NO:1.

7. (Original): The method of claim 3, wherein a polymorphic variation is detected at position 118712 in SEQ ID NO:1.

8. (Original): The method of claim 3, wherein a polymorphic variation is detected at position 98846 in SEQ ID NO:1.

9. (Original): The method of claim 3, wherein a polymorphic variation is detected at position 80400 in SEQ ID NO:1.

10. (Original): The method of claim 3, wherein the one or more polymorphic variations are detected at one or more positions in linkage disequilibrium with one or more positions in SEQ ID NO: 1 selected from the group consisting of 146311, 138875, 132526, 128002, 118712, 98846, 98682, 87826, 80400, 76779, 68398 and 64547.

11. (Original): The method of claim 3, wherein the polymorphic variation is the haplotype CTTG corresponding to positions 146311, 138875, 76779, and 68398, respectively, in SEQ ID NO: 1.

12. (Original): The method of claim 3, wherein the polymorphic variation is the haplotype ATGA corresponding to positions 146311, 138875, 76779, and 68398, respectively, in SEQ ID NO: 1.

13. (Original): The method of claim 1, wherein detecting the presence or absence of the one or more polymorphic variations comprises:

hybridizing an oligonucleotide to the nucleic acid sample, wherein the oligonucleotide is complementary to a nucleotide sequence in the nucleic acid and hybridizes to a region adjacent to the polymorphic variation;

extending the oligonucleotide in the presence of one or more nucleotides, yielding extension products; and

detecting the presence or absence of a polymorphic variation in the extension products.

14. (Currently Amended): The method of claim 13, wherein the oligonucleotide is selected from the group consisting of GTAATGTTGAACTACAATTACCA (SEQ ID NO: 45); GAAACAGGCTTCAATTCATCTT (SEQ ID NO: 46); ACATAGAGGCAGGACTGTCA (SEQ ID NO: 47); ATTAGGACATGGCTGAGATATTCA (SEQ ID NO: 48); GGACTCTGCTTATTCTACCCA (SEQ ID NO: 49); AGAGATTGTGCTTCCCAAATC (SEQ ID NO: 50); GAATTAGTGAAGTCTGGAAAGT (SEQ ID NO: 51); GAAATATGTTTGGAAAATTGTTCT (SEQ ID NO: 52); CTACAAAGCAAGACAGGACTAA (SEQ ID NO: 53); CCAAGATAAGAATCTGTTTTACC (SEQ ID NO: 54); AATGTTCTGAATTTTCCAATAA (SEQ ID NO: 55); and TTATAATTTAGTGGGGAACAGAA (SEQ ID NO: 56).

15. (Original): The method of claim 1, wherein the subject is a human.

16. (Original): A method for identifying a polymorphic variation associated with melanoma proximal to an incident polymorphic variation associated with melanoma, which comprises:

identifying a polymorphic variation proximal to the incident polymorphic variation associated with melanoma, wherein the polymorphic variation is detected in a nucleotide sequence selected from the group consisting of:

- (a) the nucleotide sequence of SEQ ID NO: 1;
- (b) a nucleotide sequence which encodes a polypeptide consisting of the amino acid sequence set forth in Figures 2A to 2G and Figure 3B;
- (c) a nucleotide sequence which encodes a polypeptide that is 90% or more identical to the amino acid sequence set forth in Figures 2A to 2G and Figure 3B; and
- (d) a fragment of a nucleotide sequence of (a), (b), or (c) comprising the polymorphic variation;

determining the presence or absence of an association of the proximal polymorphic variant with melanoma.

17. (Original): The method of claim 16, wherein the incident polymorphic variation is at a position in SEQ ID NO: 1 selected from the group consisting of 146311, 138875, 132526, 128002, 118712, 98846, 98682, 87826, 80400, 76779, 68398 and 64547.

18. (Original): The method of claim 16, wherein the proximal polymorphic variation is within a region between about 5 kb 5' of the incident polymorphic variation and about 5 kb 3' of the incident polymorphic variation.

19. (Original): The method of claim 16, which further comprises determining whether the proximal polymorphic variation is in linkage disequilibrium with the incident polymorphic variation.

20. (Original): The method of claim 16, which further comprises identifying a second polymorphic variation proximal to the identified proximal polymorphic variation associated with melanoma and determining if the second proximal polymorphic variation is associated with melanoma.

21. (Original): The method of claim 20, wherein the second proximal polymorphic variant is within a region between about 5 kb 5' of the incident polymorphic variation and about 5 kb 3' of the proximal polymorphic variation associated with melanoma.

22. (Original): An isolated nucleic acid comprising a nucleotide sequence selected from the group consisting of:

- (a) the nucleotide sequence of SEQ ID NO:1;
- (b) a nucleotide sequence which encodes a polypeptide consisting of an amino acid sequence set forth in Figures 2A-2G and Figure 3B;
- (c) a nucleotide sequence which encodes a polypeptide that is 90% or more identical to an amino acid sequence set forth in Figures 2A-2G and Figure 3B;
- (d) a fragment of a nucleotide sequence of (a), (b), or (c); and
- (e) a nucleotide sequence complementary to the nucleotide sequences of (a), (b), (c), or (d);

wherein the nucleotide sequence comprises an adenine at position 146311 of SEQ ID NO:1; the haplotype CTTG corresponding to positions 146311, 138875, 76779, and 68398, respectively, in SEQ ID NO: 1; the haplotype ATGA corresponding to positions 146311, 138875, 76779, and 68398, respectively, in SEQ ID NO: 1; and the haplotype GATTCGCATACC corresponding to positions 146311, 138875, 132526, 128002, 118712, 98846, 98682, 87826, 80400, 76779, 68398 and 64547, respectively, of SEQ ID NO: 1.

23. (Original): An oligonucleotide comprising a nucleotide sequence complementary to a portion of the nucleotide sequence of (a), (b), (c), or (d) in claim 22, wherein the 3' end of the oligonucleotide is adjacent to a polymorphic variation associated with melanoma.

24. (Currently Amended): The oligonucleotide of claim 23, which consists of a nucleotide sequence selected from the group consisting of GTAATGTTGAAACTACAATTACCA (SEQ ID NO: 45); GAAACAGGCTTCAATTCATCTT (SEQ ID NO: 46); ACATAGAGGCAGGACTGTCA (SEQ ID NO: 47); ATTAGGACATGGCTGAGATATTCA (SEQ ID NO: 48); GGAAGCTGCTTATTCTACCCA (SEQ ID NO: 49); AGAGATTGTGCTTCCCAAATC (SEQ ID NO: 50); GAATTAGTGAAGCTCTGGAAAGT (SEQ ID NO: 51); GAAATATGTTTGGAAAATTGTTCT (SEQ ID NO: 52); CTACAAAGCAAGACAGGACTAA (SEQ ID NO: 53); CCAAGATAAGAATCTGTTTACC (SEQ ID NO: 54); AATGTTCTGAATTTTCCAACTAA (SEQ ID NO: 55); and TTATAATTTAGTGGGGAACAGAA (SEQ ID NO: 56).

25. (Original): A microarray comprising an isolated nucleic acid of claim 22 linked to a solid support.

26. (Original): An isolated polypeptide encoded by the isolated nucleic acid sequence of claim 22.

27. (Original): A method for identifying a candidate molecule that modulates cell proliferation, which comprises:

(a) introducing a test molecule to a system which comprises a nucleic acid comprising a nucleotide sequence selected from the group consisting of:

- (i) the nucleotide sequence of SEQ ID NO:1;
- (ii) a nucleotide sequence which encodes a polypeptide consisting of the amino acid sequence set forth in Figures 2A to 2G and Figure 3B;
- (iii) a nucleotide sequence which encodes a polypeptide that is 90% or more identical to the amino acid sequence set forth in Figures 2A to 2G and Figure 3B; and
- (iv) a fragment of a nucleotide sequence of (i), (ii), or (iii); or

introducing a test molecule to a system which comprises a protein encoded by a nucleotide sequence of (i), (ii), (iii), or (iv); and

(b) determining the presence or absence of an interaction between the test molecule and the nucleic acid or protein,

whereby the presence of an interaction between the test molecule and the nucleic acid or protein identifies the test molecule as a candidate molecule that modulates cell proliferation.

28. (Original): The method of claim 27, wherein the system is an animal.

29. (Original): The method of claim 27, wherein the system is a cell.

30. (Original): The method of claim 27, wherein the nucleotide sequence comprises one or more polymorphic variations associated with melanoma.

31. (Original): The method of claim 30, wherein the nucleotide sequence comprises a polymorphic variation associated with melanoma at one or more positions in SEQ ID NO: 1 selected from the group consisting of 146311, 138875, 132526, 128002, 118712, 98846, 98682, 87826, 80400, 76779, 68398 and 64547.

32. (Original): A method for treating melanoma in a subject, which comprises administering a candidate molecule identified by the method of claim 27 to a subject in need thereof, whereby the candidate molecule treats melanoma in the subject.

33. (Original): A method for identifying a candidate therapeutic for treating melanoma, which comprises:

(a) introducing a test molecule to a system which comprises a nucleic acid comprising a nucleotide sequence selected from the group consisting of:

- (i) the nucleotide sequence of SEQ ID NO:1;
- (ii) a nucleotide sequence which encodes a polypeptide consisting of the amino acid sequence set forth in Figures 2A to 2G and Figure 3B;
- (iii) a nucleotide sequence which encodes a polypeptide that is 90% or more identical to the amino acid sequence set forth in Figures 2A to 2G and Figure 3B; and

(iv) a fragment of a nucleotide sequence of (i), (ii), or (iii); or
introducing a test molecule to a system which comprises a protein encoded by a nucleotide sequence of (i), (ii), (iii), or (iv); and
(b) determining the presence or absence of an interaction between the test molecule and the nucleic acid or protein,
whereby the presence of an interaction between the test molecule and the nucleic acid or protein identifies the test molecule as a candidate therapeutic for treating melanoma.

34. (Original): A method for treating melanoma in a subject, which comprises contacting one or more cells of a subject in need thereof with a nucleic acid, wherein the nucleic acid comprises a nucleotide sequence selected from the group consisting of:

- (a) the nucleotide sequence of SEQ ID NO:1;
- (b) a nucleotide sequence which encodes a polypeptide consisting of the amino acid sequence set forth in Figures 2A to 2G and Figure 3B;
- (c) a nucleotide sequence which encodes a polypeptide that is 90% or more identical to the amino acid sequence set forth in Figures 2A to 2G and Figure 3B;
- (d) a fragment of a nucleotide sequence of (a), (b), or (c); and
- (e) a nucleotide sequence complementary to the nucleotide sequence of (a), (b), (c), or (d);

whereby contacting the one or more cells of the subject with the nucleic acid treats melanoma in the subject.

35. (Original): The method of claim 33, wherein the nucleic acid is duplex RNA.

36. (Currently Amended): The method of claim 34, wherein the duplex RNA comprises a strand comprising the nucleotide sequence ATATATCTGGAGGCCTATG (SEQ ID NO: 57); GCTAGATGCACTCCAACAA (SEQ ID NO: 58); TTACCTGGCTCACTAACTA (SEQ ID NO: 59); or ACTAACGTGAAAGCCTTAC (SEQ ID NO: 60).

37. (Original): A method for treating melanoma in a subject, which comprises contacting one or more cells of a subject in need thereof with a protein, wherein the protein is encoded by a nucleotide sequence which comprises a polynucleotide sequence selected from the group consisting of:

- (a) the polynucleotide sequence of SEQ ID NO:1;
- (b) a polynucleotide sequence which encodes a polypeptide consisting of the amino acid sequence set forth in Figures 2A to 2G and Figure 3B;
- (c) a polynucleotide sequence which encodes a polypeptide that is 90% or more identical to the amino acid sequence set forth in Figures 2A to 2G and Figure 3B; and
- (d) a fragment of a polynucleotide sequence of (a), (b), or (c);

whereby contacting the one or more cells of the subject with the protein treats melanoma in the subject.

38. (Original): A method for treating melanoma in a subject, which comprises:
detecting the presence or absence of one or more polymorphic variations associated with melanoma in a nucleic acid sample from a subject, wherein the polymorphic variation is detected in a nucleotide sequence selected from the group consisting of:

- (a) the nucleotide sequence of SEQ ID NO:1;
- (b) a nucleotide sequence which encodes a polypeptide consisting of the amino acid sequence set forth in Figures 2A to 2G and Figure 3B;
- (c) a nucleotide sequence which encodes a polypeptide that is 90% or more identical to the amino acid sequence set forth in Figures 2A to 2G and Figure 3B; and
- (d) a fragment of a nucleotide sequence of (a), (b), or (c) comprising the polymorphic variation; and

administering a melanoma treatment to a subject in need thereof based upon the presence or absence of the one or more polymorphic variations in the nucleic acid sample.

39. (Original): The method of claim 38, wherein the one or more polymorphic variations are detected at one or more positions in SEQ ID NO: 1 selected from the group consisting of 146311, 138875, 132526, 128002, 118712, 98846, 98682, 87826, 80400, 76779, 68398 and 64547.

40. (Original): The method of claim 38, which further comprises extracting and analyzing a tissue biopsy sample from the subject.

41. (Original): The method of claim 38, wherein the treatment is one or more selected from the group consisting of administering cisplatin, administering carmustine, administering vinblastine, administering vincristine, administering bleomycin, administering a combination of the foregoing, and surgery.

42. (Original): A method for preventing melanoma in a subject, which comprises:
detecting the presence or absence of one or more polymorphic variations associated with melanoma in a nucleic acid sample from a subject, wherein the polymorphic variation is detected in a nucleotide sequence selected from the group consisting of:

- (a) the nucleotide sequence of SEQ ID NO:1;
- (b) a nucleotide sequence which encodes a polypeptide consisting of the amino acid sequence set forth in Figures 2A to 2G and Figure 3B;
- (c) a nucleotide sequence which encodes a polypeptide that is 90% or more identical to the amino acid sequence set forth in Figures 2A to 2G and Figure 3B; and
- (d) a fragment of a nucleotide sequence of (a), (b), or (c) comprising the polymorphic variation; and

administering a melanoma preventative to a subject in need thereof based upon the presence or absence of the one or more polymorphic variations in the nucleic acid sample.

43. (Original): The method of claim 42, wherein the one or more polymorphic variations are detected at one or more positions in SEQ ID NO: 1 selected from the group consisting of 146311, 138875, 132526, 128002, 118712, 98846, 98682, 87826, 80400, 76779, 68398 and 64547.

44. (Original): The method of claim 42, wherein the preventative reduces ultraviolet (UV) light exposure to the subject.

45. (Original): A method of targeting information for preventing or treating melanoma to a subject in need thereof, which comprises:
detecting the presence or absence of one or more polymorphic variations associated with melanoma in a nucleic acid sample from a subject, wherein the polymorphic variation is detected in a nucleotide sequence selected from the group consisting of:

- (a) the nucleotide sequence of SEQ ID NO:1;
 - (b) a nucleotide sequence which encodes a polypeptide consisting of the amino acid sequence set forth in Figures 2A to 2G and Figure 3B;
 - (c) a nucleotide sequence which encodes a polypeptide that is 90% or more identical to the amino acid sequence set forth in Figures 2A to 2G and Figure 3B; and
 - (d) a fragment of a nucleotide sequence of (a), (b), or (c) comprising the polymorphic variation; and
- directing information for preventing or treating melanoma to a subject in need thereof based upon the presence or absence of the one or more polymorphic variations in the nucleic acid sample.

46. (Original): The method of claim 45, wherein the one or more polymorphic variations are detected at one or more positions in SEQ ID NO: 1 selected from the group consisting of 146311, 138875, 132526, 128002, 118712, 98846, 98682, 87826, 80400, 76779, 68398 and 64547.

47. (Original): The method of claim 45, wherein the information comprises a description of methods for reducing ultraviolet (UV) light exposure to the subject.

48. (Original): The method of claim 45, wherein the information comprises a description of chemotherapeutic treatments and surgical treatments of melanoma.